



US008598219B2

(12) **United States Patent**
Calderari et al.

(10) **Patent No.:** US 8,598,219 B2
(45) **Date of Patent:** *Dec. 3, 2013

(54) **LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSERTRON**

(71) Applicants: **Helsinn Healthcare S.A.**, Lugano (CH);
Roche Palo Alto LLC, Palo Alto, CA (US); **Simone Macciocchi**, Melide (CH); **Giulio Macciocchi**, Breganzona (CH)

(72) Inventors: **Giorgio Calderari**, Rancate (CH);
Daniele Bonadeo, Casalzuigno (IT);
Roberta Cannella, Varese (IT); **Alberto Macciocchi**, Melide (CH); **Andrew Miksztal**, Palo Alto, CA (US); **Thomas Malefyt**, Carmel Valley, CA (US); **Kathleen M Lee**, Palo Alto, CA (US); **Carmine Panuccio**, Casnate con Bernat (IT)

(73) Assignees: **Helsinn Healthcare SA**,
Lugano/Pazzallo (CH); **Roche Palo Alto LLC**, Palo Alto, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: 13/901,437

(22) Filed: May 23, 2013

(65) **Prior Publication Data**

US 2013/0261592 A1 Oct. 3, 2013

Related U.S. Application Data

(63) Continuation-in-part of application No. 13/087,012, filed on Apr. 14, 2011, now Pat. No. 8,518,981, which is a continuation of application No. 11/186,311, filed on Jul. 21, 2005, now Pat. No. 7,947,724, which is a continuation of application No. PCT/EP2004/000888, filed on Jan. 30, 2004.

(60) Provisional application No. 60/444,351, filed on Jan. 30, 2003.

(51) **Int. Cl.**

A01N 43/52 (2006.01)

(52) **U.S. Cl.**

USPC 514/397

(58) **Field of Classification Search**

USPC 514/397

See application file for complete search history.

(56) **References Cited****U.S. PATENT DOCUMENTS**

4,695,578 A	9/1987	Coates et al.
4,753,789 A	6/1988	Tyers et al.
4,886,808 A	12/1989	King
4,906,755 A	3/1990	Gittos
4,929,632 A	5/1990	Tyers et al.
4,937,247 A	6/1990	King

5,011,846 A	4/1991	Gittos et al.
5,034,398 A	7/1991	King
5,202,333 A	4/1993	Berger et al.
5,240,954 A	8/1993	Tyers et al.
5,272,137 A	12/1993	Blase et al.
5,344,658 A	9/1994	Collin
5,578,628 A	11/1996	Tyers et al.
5,578,632 A	11/1996	Tyers et al.
5,622,720 A	4/1997	Collin
5,854,270 A	12/1998	Gambhir
5,922,749 A	7/1999	Tyers et al.
5,955,488 A	9/1999	Winterborn
6,063,802 A	5/2000	Winterborn
6,132,758 A	10/2000	Munayyer et al.
6,284,749 B1	9/2001	Castillo et al.
6,287,592 B1	9/2001	Dickinson
6,294,548 B1	9/2001	James
6,699,852 B2	3/2004	Robichaud
7,109,339 B2	9/2006	Lee et al.
7,947,724 B2	5/2011	Calderari et al.
7,947,725 B2	5/2011	Calderari et al.
7,960,424 B2	6/2011	Calderari et al.
8,518,981 B2	8/2013	Calderari et al.
2001/002009 A1	9/2001	James
2003/0095926 A1	5/2003	Dugger, III

FOREIGN PATENT DOCUMENTS

EP	0 512 400 A1	4/1992
WO	WO-03100091	12/2003
WO	WO-2004045615	6/2004
WO	WO-2004067005	8/2004
WO	WO-2004703714	9/2004

OTHER PUBLICATIONS

Center for Drug Evaluation and Research (Sep. 2002).*
R. M. Eglen et al., "Pharmacological characterization of RS 25259-197, a novel and selective 5-HT3 receptor antagonist, *in vivo*," Br. J Pharmacology 114:860-866 (1995).
Chelly, Jacques et al., Oral RS-25259 Prevents Postoperative Nausea and Vomiting Following Laparoscopic Surgery, Anesthesiology, 1996, vol. 85, No. 3A, p. A21.
Sorbe, Bengt, 5-HT-3 Receptor Antagonists as Antiemetic Agents in Cancer Chemotherapy, extracted from Expert Opinion on Investigational Drugs, 1996, vol. 5 No. 4, pp. 389-407.
Gaster, Laramie M. and King, Frank D., Serotonin 5-HT3 and 5-HT4 Receptor Antagonists, extracted from Medicinal Research Reviews, 1997 vol. 17, No. 2, pp. 163-214.
Tang, Jun et al., "Efficacy of RS-25259, a Novel 5-HT3 Antagonist, In the Prevention of Postoperative Nausea and Vomiting after Major Gynecologic Surgery," Anesthesiology, 1997, vol. 85, No. 3 suppl. p. A329.
Tang, Jun et al., The Efficacy of RS-25259, a Long-Acting Selective 5-HT3 Receptor Antagonist, for Preventing Postoperative Nausea and Vomiting After Hysterectomy Procedures, Anesthesia and Analgesia, 1998, vol. 87, pp. 462-467.
Adis R&D Profile, Palonosetron RS 25259 197, Drugs in R&D, Oct. 1999, vol. 2, No. 4, pp. 251-252.

(Continued)

Primary Examiner — Shirley Gembeh

(74) *Attorney, Agent, or Firm* — Clark G. Sullivan; Troutman Sanders LLP

ABSTRACT

The present invention relates to shelf-stable liquid formulations of palonosetron for reducing chemotherapy and radiotherapy induced emesis with palonosetron. The formulations are particularly useful in the preparation of intravenous and oral liquid medicaments.

8 Claims, No Drawings